

Supplemental Amendment and Response
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Amendments to the Claims:

Prior to further substantive examination, please cancel claims 38, 41-43, and 74-98 without prejudice to their subsequent reintroduction into this application or their introduction into a related application. Claims 74-98 were previously withdrawn; however, these claims have been cancelled in this amendment. Claims 37, 39, and 40 have been amended. Upon entry of this paper, claims 33, 36, 37, 39, 40, 44-54, 56-62, and 107 will be pending and under consideration in this case.

The following listing of claims replaces all prior versions and lists of claims in the application:

Listing of Claims:

1-32. (Cancelled)

33. (Previously Presented) A method of identifying a molecule that binds to a large ribosomal subunit, the method comprising the steps of:

- (a) providing a molecular model comprising one or more target regions selected from the group consisting of at least a portion of (i) a peptidyl transferase site, (ii) an A-site, (iii) a P-site, (iv) an E-site, (v) an elongation factor binding domain, (vi) a polypeptide exit tunnel, and (vii) a signal recognition particle (SRP) binding domain, from the atomic co-ordinates for *Haloarcula marismortui* large ribosomal subunit found on Disk 1 under file name 1JJ2.RTF, 1JJ2.TXT, 1JJ2.PDB, PDB1FFK.DOC, or PDB1FFK.ENT, or deposited at the Protein Data Bank under accession number PDB ID: 1JJ2 or 1FFK, or derived from said *Haloarcula marismortui* atomic co-ordinates by molecular modeling;
- (b) using the molecular model to identify a candidate molecule that can bind to the one or more target regions in the molecular model; and
- (c) producing the candidate molecule identified in step (b).

34-35. (Cancelled)

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36. (Previously Presented) The method of claim 33, comprising the additional step of determining whether the candidate molecule modulates ribosomal activity.
37. (Currently Amended) The method of claim 36, comprising the additional step of repeating ~~one or more~~ of steps (a) through (c) to identify and produce a modified candidate molecule having higher binding specificity, higher binding affinity or higher potency relative to the candidate molecule.
38. (Cancelled)
39. (Currently Amended) The method of claim [[38]] 37, comprising the additional step of determining whether the modified candidate molecule modulates ribosomal activity.
40. (Currently Amended) The method of claim 39, comprising the additional step of, after determining whether the modified candidate molecule modulates ribosomal activity, producing a large quantity of the modified candidate molecule that modulates ribosomal activity.
- 41.-43. (Cancelled)
44. (Previously Presented) The method of claim 33, wherein the ~~one or more~~ target regions comprises at least a portion of an active site.
45. (Original) The method of claim 44, wherein the active site comprises at least a portion of a peptidyl transferase site.
46. (Original) The method of claim 44, wherein the peptidyl transferase site is defined by a plurality of residues set forth in Table 5A or Table 5B.
47. (Previously Presented) The method of claim 33, wherein the ~~one or more~~ target regions comprises at least a portion of an A-site.
48. (Original) The method of claim 47, wherein the A-site is defined by a plurality of residues set forth in Table 6A or Table 6B.

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49. (Previously Presented) The method of claim 33 or 47, wherein the one or more target regions comprises a least a portion of a P-site.
50. (Original) The method of claim 49, wherein the P-site is defined by a plurality of residues set forth in Table 7A or Table 7B.
51. (Previously Presented) The method of claim 33 or 47, wherein the one or more target regions comprises at least a portion of a polypeptide exit tunnel.
52. (Original) The method of claim 51, wherein the exit tunnel is defined by a plurality of residues set forth in Table 8A, Table 8B, Table 9, or Table 10.
53. (Previously Presented) The method of claim 49, wherein the one or more target regions comprises at least a portion of a polypeptide exit tunnel.
54. (Original) The method of claim 53, wherein the exit tunnel is defined by a plurality of residues set forth in Table 8A, Table 8B, Table 9, or Table 10.
55. (Cancelled)
56. (Original) The method of claim 33, wherein the molecular model is in an electronic form.
57. (Original) The method of claim 33, wherein the molecular model is generated from atomic co-ordinates produced by molecular modeling.
58. (Previously Presented) The method of claim 33 or 57, wherein the molecular model is generated from atomic co-ordinates produced by homology modeling using at least a portion of the atomic co-ordinates deposited at the Protein Data Bank under accession number PDB ID: 1FFK, 1FFZ, 1FG0, 1JJ2, or recorded on Disk No. 1 under file name PDB1FFK.DOC, PDB1FFK.ENT, PDB1FFZ.DOC, PDB1FFZ.ENT, PDB1FG0.DOC, PDB1FG0.ENT, 1JJ2.RTF, 1JJ2.TXT, or 1JJ2.PDB.
59. (Previously Presented) The method of claim 33 or 57, wherein the molecular model is generated from atomic co-ordinates produced by molecular replacement using at least a portion of the atomic co-ordinates deposited at the Protein Data Bank under accession

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number PDB ID: 1FFK, 1FFZ, 1FG0, 1JJ2, or recorded on Disk No. 1 under file name PDB1FFK.DOC, PDB1FFK.ENT, PDB1FFZ.DOC, PDB1FFZ.ENT, PDB1FG0.DOC, PDB1FG0.ENT, 1JJ2.RTF, 1JJ2.TXT, or 1JJ2.PDB.

60. (Original) The method of claim 33, wherein the molecular model comprises residues that are conserved among one or more prokaryotic organisms.
61. (Original) The method of claim 33, wherein the molecular model comprises a residue that is present in a prokaryotic ribosome but is absent from a eukaryotic ribosome or a eukaryotic mitochondrial ribosome.
62. (Original) The method of claim 61, wherein the eukaryotic ribosome is a mammalian ribosome.

63-106. (Cancelled)

107. (Previously Presented) A method of identifying a molecule that binds to a large ribosomal subunit, the method comprising the steps of:
 - (a) providing a molecular model comprising one or more target regions selected from the group consisting of a peptidyl transferase site, an A-site, a P-site, an E-site, an elongation factor binding domain, a polypeptide exit tunnel, and a signal recognition particle (SRP) binding domain, from the atomic co-ordinates (i) for *Haloarcula marismortui* large ribosomal subunit found on Disk 1 under file name 1JJ2.RTF, 1JJ2.TXT, 1JJ2.PDB, PDB1FFK.DOC, or PDB1FFK.ENT, or deposited at the Protein Data Bank under accession number PDB ID: 1JJ2 or 1FFK, or (ii) derived from the *Haloarcula marismortui* atomic co-ordinates by molecular modeling;
 - (b) using the molecular model to identify a candidate molecule that can bind to the one or more target regions in the molecular model; and
 - (c) producing the candidate molecule identified in step (b).